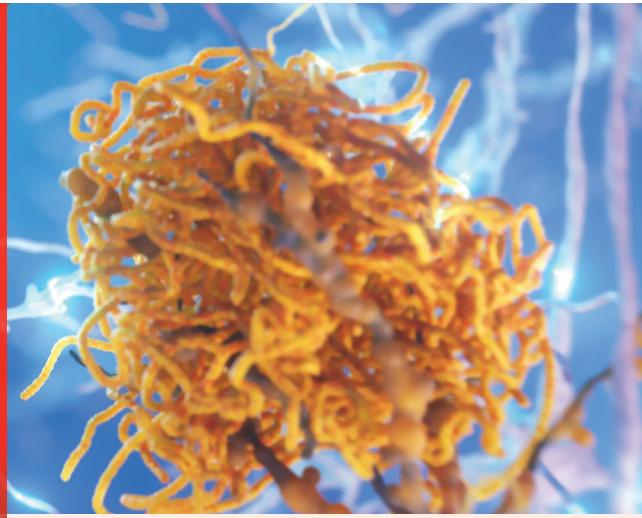


What do amyloid and tau biomarkers tell us about cognitive decline in asymptomatic older adults?



Alzheimer's disease (AD) is a progressive neurodegenerative disorder associated with cognitive, functional, and behavioral impairments.^{1,2}

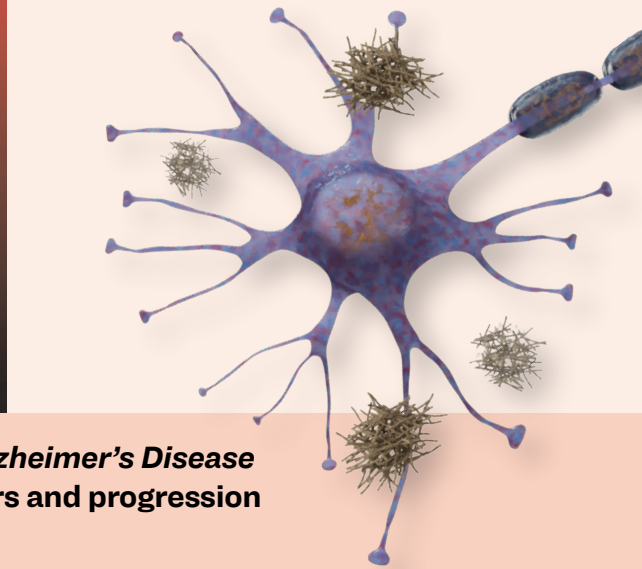


The hallmark features of AD include β -amyloid plaques and tau neurofibrillary tangles which are thought to drive neurodegeneration.¹⁻³



AD-related pathology accumulates decades before cognitive symptoms appear in a phase of the disease called preclinical AD.^{1,2,4}

➤ These individuals are at high risk for developing cognitive symptoms



A recent study* published in the *Journal of Prevention of Alzheimer's Disease* reported on the relationship between AD-related biomarkers and progression from preclinical to symptomatic stages.⁵



Study design^{5†}

The study used data from the Phase 3 Anti-Amyloid Treatment in Asymptomatic Alzheimer's disease (A4) trial as well as its companion study, the Longitudinal Evaluation of Amyloid and Neurodegeneration Risk (LEARN) study.

Together, these studies enrolled over 1700 participants ages 65-85 who:



Were cognitively unimpaired at baseline



Were in overall good health



Had a study partner familiar with their cognitive function



Had varying levels of amyloid pathology measured via baseline PET

Elevated Amyloid

A4 Trial

Negative Amyloid

LEARN Study

Researchers explored whether baseline levels of amyloid PET, plasma P-tau217, and tau PET (subset of participants) could predict cognitive and functional outcomes over ~4.5 years.

More on biomarkers^{4,5}

Amyloid PET imaging

- Measures amyloid plaques in the brain; abnormal amyloid plaque deposition is thought to be the first neuropathological sign of AD

Plasma P-tau217

- Primarily reflects amyloid plaque burden
- Also reflects an early stage of tau phosphorylation contributing to the misfolding process that results in tau neurofibrillary tangle formation
 - May also reflect the degree to which amyloid is triggering downstream effects like tauopathy

Tau PET imaging

- Measures aggregated tau neurofibrillary tangles in the brain, which are thought to occur later in the process of AD; abnormal Tau PET is closely coupled with clinical symptoms and neurodegeneration



Results⁵



Select baseline participant characteristics for participants with available P-tau217 data

	A4 Trial (N=1056)	LEARN Study (N=469)
Age (years)	71.9 (4.8)	70.5 (4.3)
Female sex	617 (58.4%)	289 (61.6%)
Family history	792 (75.0%)	308 (65.7%)
Amyloid PET (Centiloids)	66.2 (32.7)	4.7 (12.4)
Plasma P-tau217	0.3 (0.2)	0.2 (0.1)



Key findings⁵



~50% of people with preclinical AD, as indicated via higher levels of AD-related biomarkers, progressed to the symptomatic stages of AD within 5 years.

- The majority of participants without AD-related pathology did not exhibit symptomatic progression

Clinical Dementia Rating-Global Score (CDR-GS) Progression by Plasma P-tau217

(Kaplan-Meier estimates)

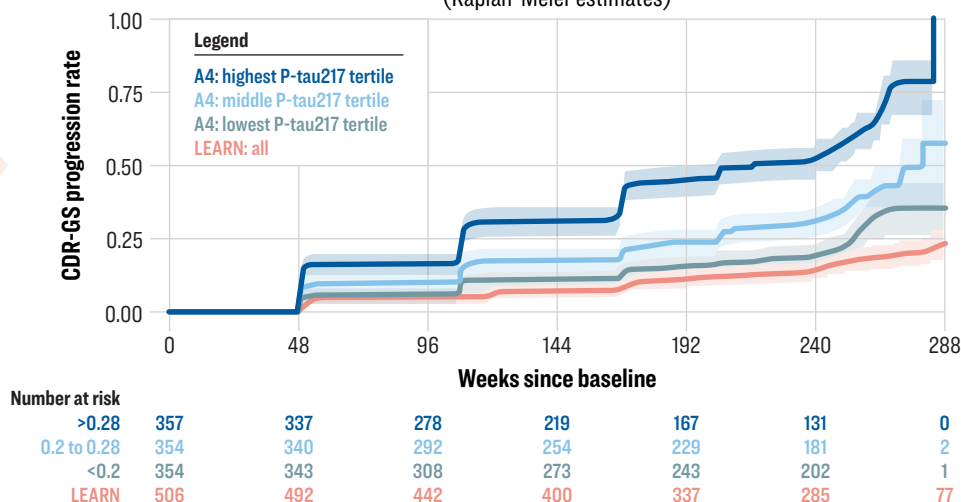


Figure modified from Sperling RA, et al.⁵

Across the entire cohort, baseline plasma P-tau217 was the strongest predictor of cognitive decline.

- In a subset of participants with tau PET imaging, neocortical tau was the strongest predictor of cognitive decline, showing that tau deposition is related to clinical deterioration



The study reported that cognitively unimpaired individuals with preclinical AD and higher levels of biomarkers such as plasma P-tau217 showed a greater risk of progressing to symptomatic AD within 5 years.



Limitations⁵

- Participants in the study may not represent a generalizable older population. They were generally in good health, volunteered and met screening criteria for the A4 clinical trial, were willing to commit to multiple visits over several years, had higher rates of family history of dementia than typical, and were predominantly White and not Hispanic or Latino
- Participants were also aware of their amyloid PET status (elevated vs not elevated), which may have influenced assessments

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PET=positron emission tomography.

1. Alzheimer's Association. *Alzheimers Dement*. 2025;21(4):e70235. 2. Porsteinsson AP, et al. *J Prev Alz Dis*. 2021;3(8):371-386.

3. Raskin J, et al. *Curr Alzheimer Res*. 2015;12(8):712-722. 4. Jack CR Jr, et al. *Alzheimers Dement*. 2024;20(8):5143-5169.

5. Sperling RA, et al. *J Prev Alz Dis*. 2024;4(1):802-813.

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